



Biodesic

hardware :: software :: wetware

Building the Bio-economy

The Context of Current Practices in Synthetic Biology

Presidential Commission for the Study of Bioethical Issues

Washington DC, July 2010

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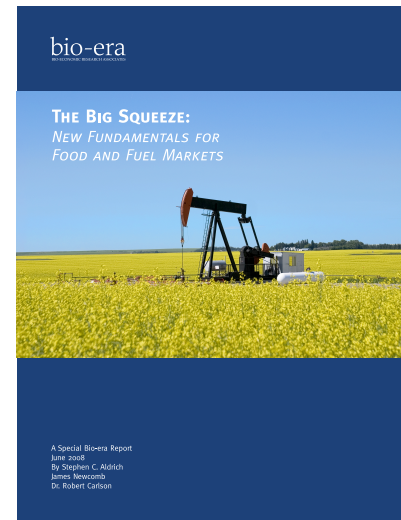
blog: www.synthesis.cc



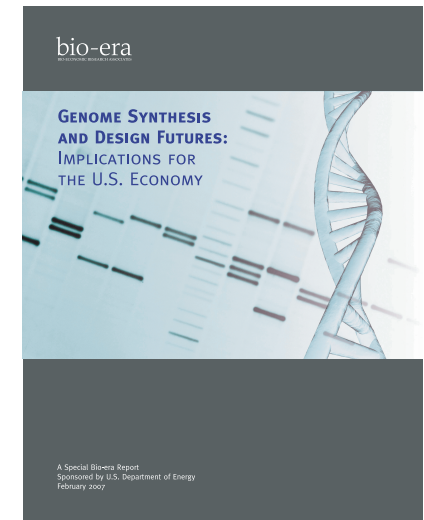
Reading



Biology is Technology: The Promise, Peril, and New Business of Engineering Life
Robert Carlson, Harvard University Press, 2010.



The Big Squeeze: New Fundamentals for Food and Fuel Markets
Stephen C. Aldrich, James Newcomb, Robert Carlson, June 2008



Genome Synthesis and Design Futures: Implications for the US Economy
James Newcomb, Robert Carlson, Stephen C. Aldrich, February 2007

- blog: www.synthesis.cc
- "The changing economics of DNA synthesis", Carlson, *Nature Biotech*, Dec 2009.
- "The market value of GM products", Carlson, *Nature Biotech*, Nov 2009.
- "Laying the foundations for a bio-economy", Carlson, *Syst Synth Biol*, 2008.
- "The pace and proliferation of biological technologies", Carlson, *Biosec Bioter*, 2003.
- "Open source biology and its impact on industry", Carlson, *IEEE Spectrum*, 2001.

Thanks to: Rik Wehbring, Jay Keasling, Drew Endy, Roger Brent, Freeman Dyson, Stewart Brand, Kevin Kelly, James Newcomb, Stephen Aldrich, John Mulligan, Sarah Keller and Pascale Carlson.



Toward Engineering Biology: ***Every Piece Has Its Purpose***

http://www.swaystudio.com/Honda_Purpose.html

A Hierarchy of Engineering and Economic Complexities



Multiple Cells: Control of growth and differentiation; products are cells and structures that cells make (Tissues, Organs, Animals, Houses).



Synthetic Single Cells: Looks initially like Metabolic Engineering; products are chemicals and biologicals made by cells.



Multiple Genes in a Single Cell Type: Metabolic Engineering: Fuels, Plastics, Terpenoids for Drugs, Flavors, and Fragrances. **RFS.**



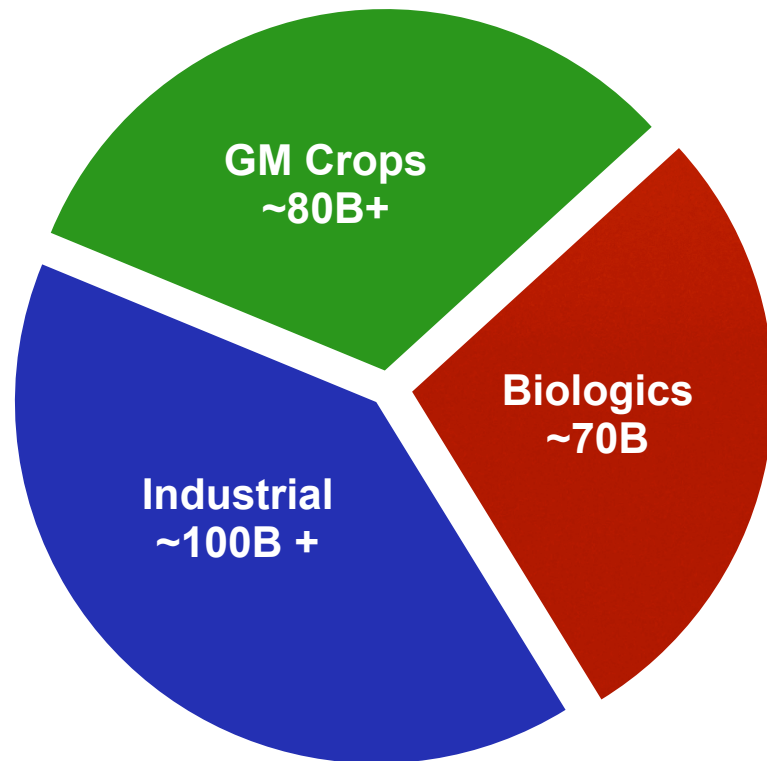
Single Gene in a Single Cell: Recombinant Proteins: Laundry Enzymes, HGH, EPO.





“Genetically Modified Stuff” in the US Bioeconomy (2010 est.): >\$250B or Equivalent of ~2% of GDP

U.S. Biotech Revenues in \$ Billions



GM revenue growth:
Crops 10%, Biologics 10%, Industrial 20%.
(Sources: *Nat Biotech*, *Forbes*, *FT*, *Bloomberg*)

Just 1/6 of 1% of workforce in U.S.
contributed >5% of GDP growth in the
years 2000 to 2007.
(Sources: BEA, *Nat Biotech*, *Biodesic*)

McKinsey and E&Y estimates for industrial
apps range from \$70B to \$140B.

US DOC value added to GDP (2007): mining 2%, construction 4.1%, information and broadcasting 4.7%, all of manufacturing 11.7%, transportation and warehousing 2.9%, finance 20.7%, and all of government 12.6%.



Global Adoption: Biotech Revenues as % of GDP

Country	2010 Biotech Revenues	2020 Target Biotech Revenues
United States	2%	NA
China	2.5% (?)	8%
Malaysia	2.5%	10%
India	1.5%	NA
Pakistan	1.4%	NA
Europe	1.3%	NA

Source: Biodesic

Main source of uncertainty is definition of “biotechnology”; i.e., all biology or only products of genetic modification.



Parsing the Spread of Biological Technologies

Drivers

**Economic
Growth/Jobs**

**Material and
Energy
Efficiencies**

**Carbon Load
Reduction**

**Curiosity
(It's cool, dude.)**

**FOOD, WATER,
ENERGY!**

Characteristics

1. International
2. Distributed
(Beer Vs. Oil)
3. Increasing Capabilities
4. Decreasing Costs
5. "Open Source"?

Consequences

1. Widespread access to tools, skills, and materials.
2. Lower environmental impact (emissions).
3. Lower energy usage.
4. Reduction in foreign energy and materials dependency.
5. More diverse bio-economy that can withstand shocks.
6. More diverse technological development for rapid countermeasures.

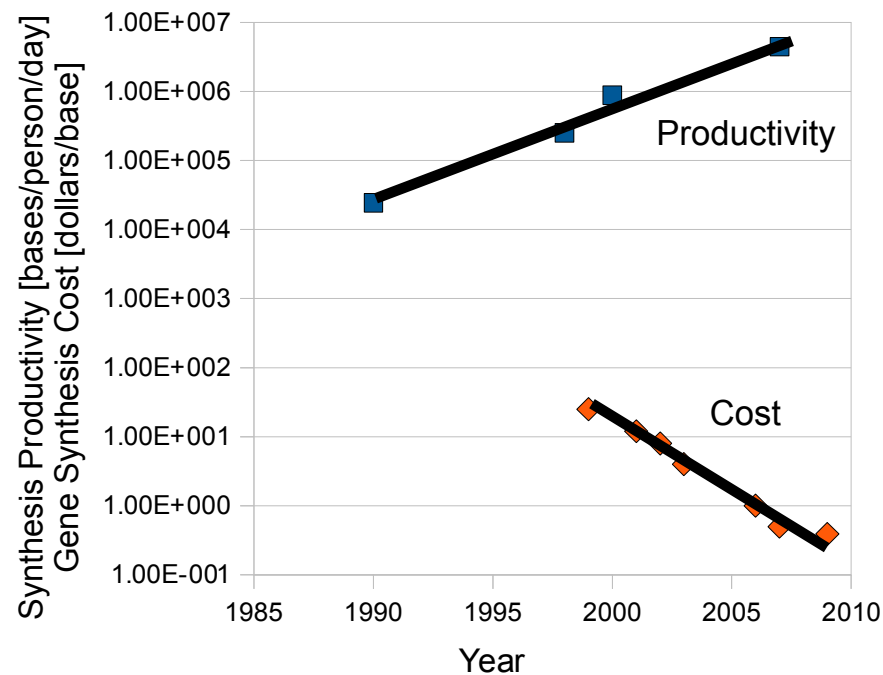
Major Uncertainties

Oil Price, Petroleum Production Investment, Gov't R&D Investment in Bio, National and Int'l Regulatory Policy, Threat Events, EU Carbon Labeling?, US Electrification?, Chinese Renewable Investment?

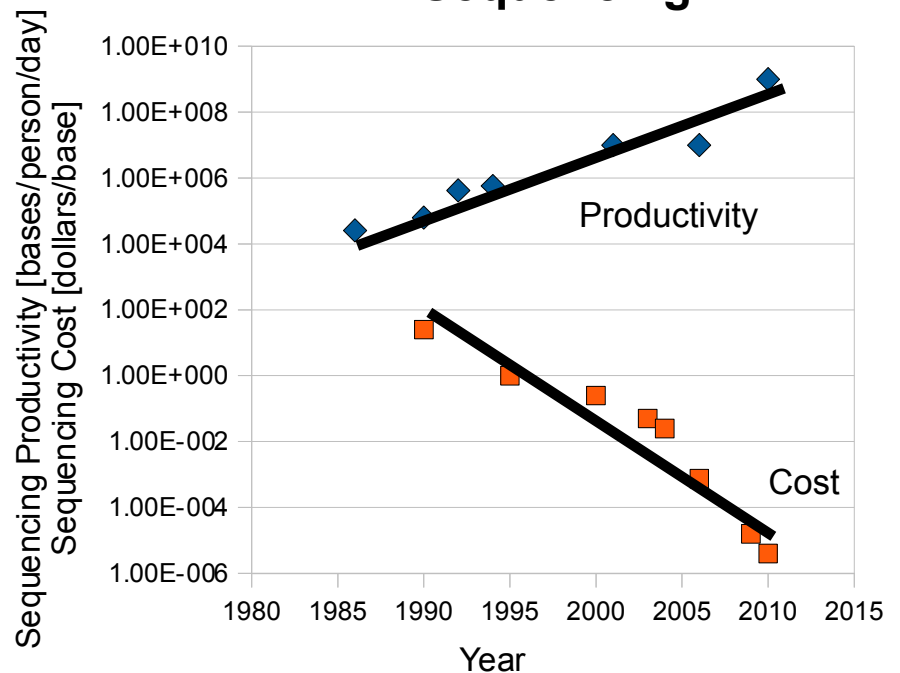


Exponential Progress in Reading DNA and Writing DNA

DNA Synthesis



DNA Sequencing

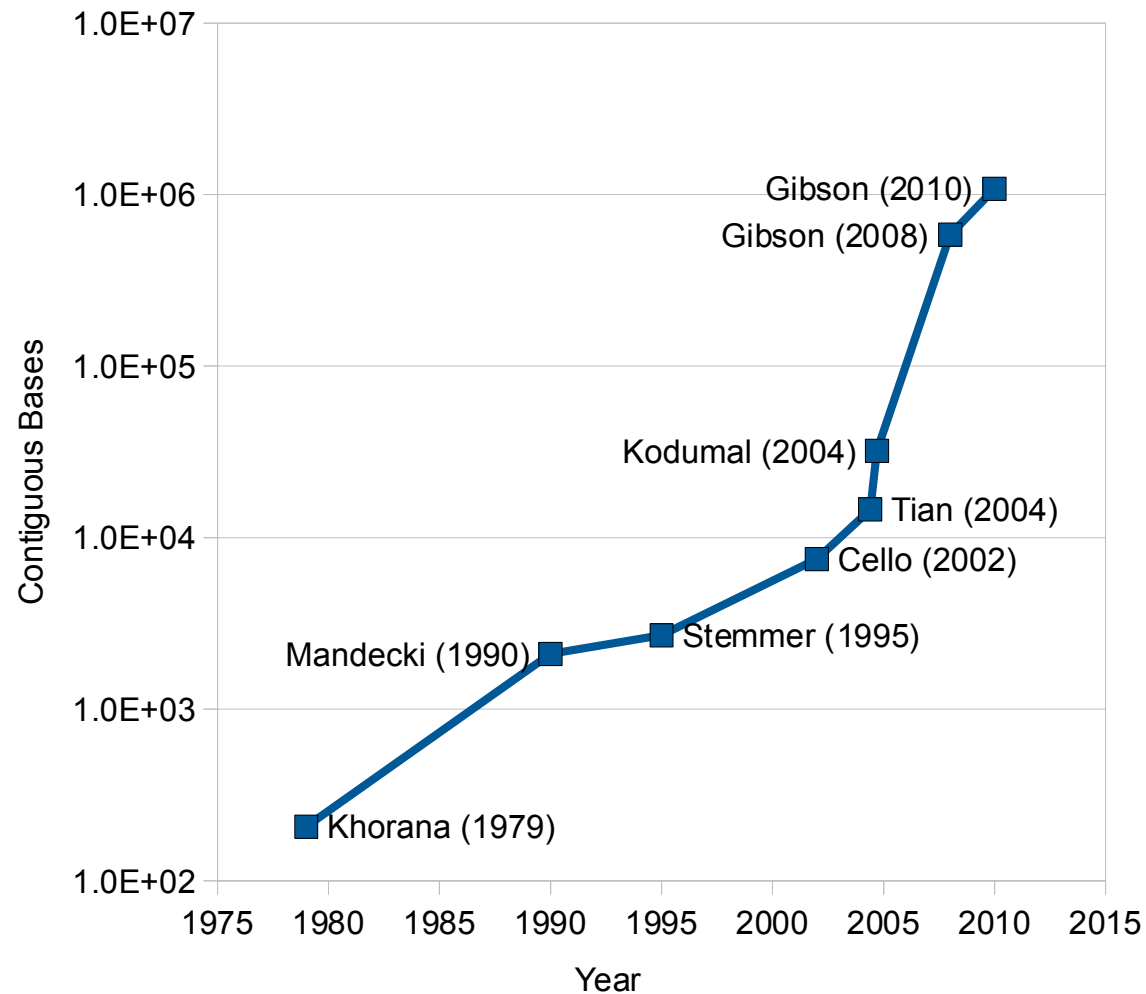


Sources: Biodesic, www.synthesis.cc



Constructing Genes and Genomes

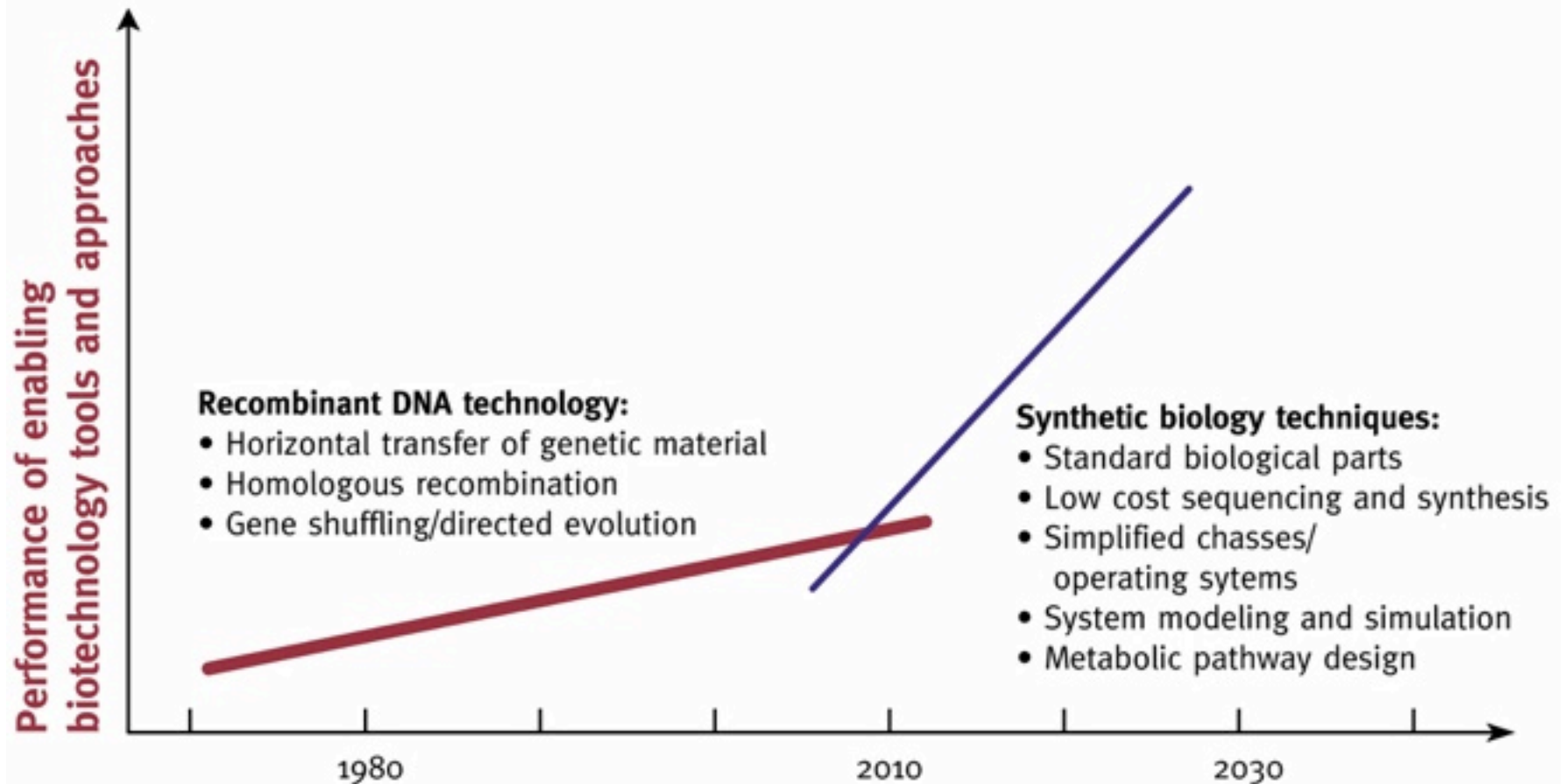
Longest Published sDNA



Sources: see <http://www.synthesis.cc/2010/05/booting-up-a-synthetic-genome-1.html>



An Inflection Point in Biotech Capabilities?

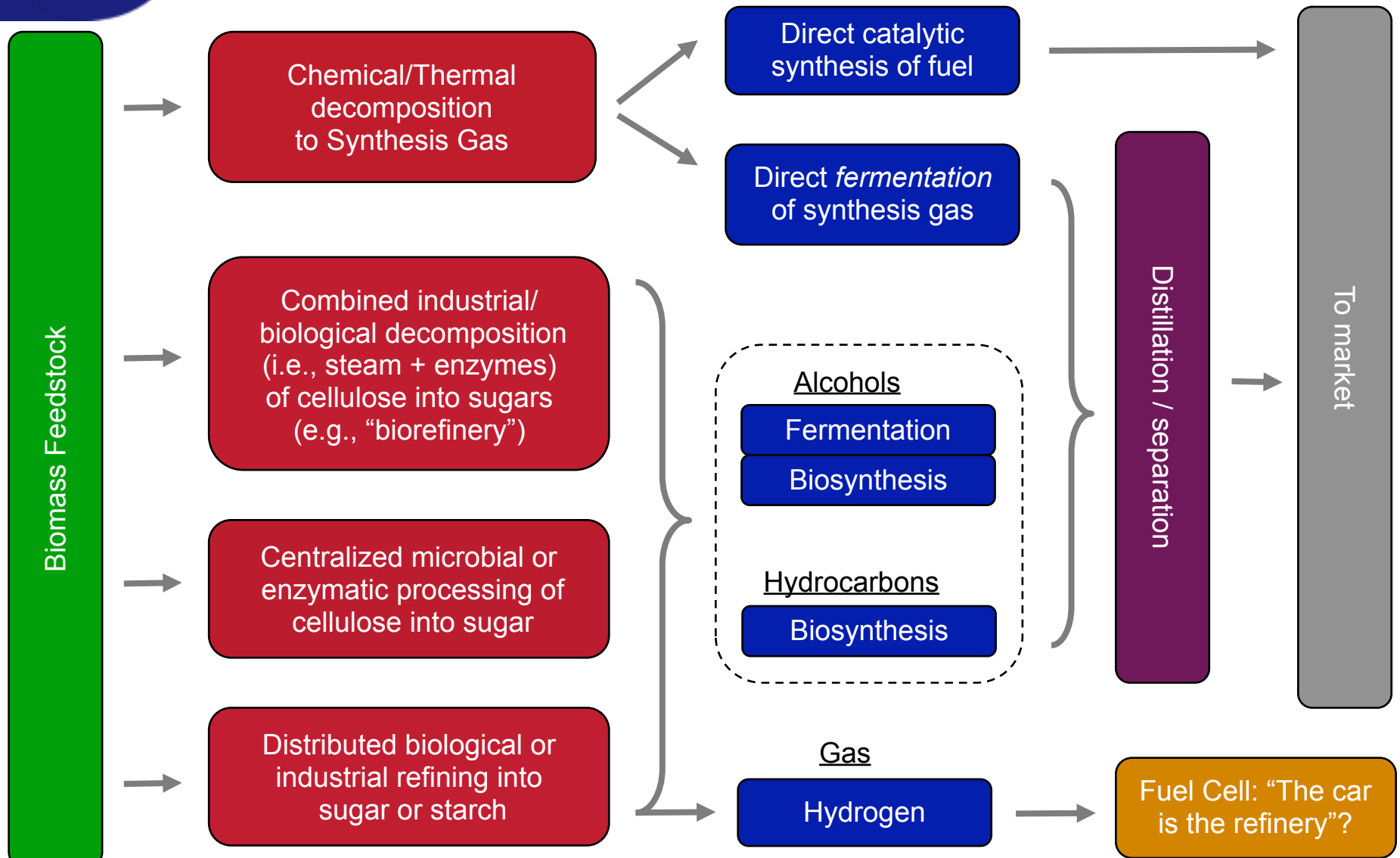


“Genome Synthesis and Design Futures: Implications for the U.S. Economy”

Bio Economic Research Associates, 2007. www.bio-era.net



Challenges I: An Increasing Diversity of Energy Sources





Challenges II: New Technologies to Address Threats

2000	Nov. 1	Ralph Baric publishes gastroenteritis RNA viral assembly method.
2002	Nov. 16	First case of atypical pneumonia reported in Guangdong, China.
2003	Feb. 26	First case of unusual pneumonia reported in Hanoi, Vietnam.
	Feb. 28	WHO officer, Dr. Carlo Urbani, examines patient.
	Mar. 10	Urbani reports outbreak to WHO headquarters.
	Mar. 11	Outbreak of mysterious respiratory disease reported in Hong Kong.
	Mar. 12	WHO issues global alert.
	Mar. 29	Urbani dies.
	Apr. 4	SARS added to US list of quarantinable diseases.
	Apr. 9	WHO team reports evidence of “super spreaders”.
	Apr. 12	Canadian researchers map SARS’ genetic sequence, achieved in six days.
	Apr. 14	CDC announces achievement of similar sequence.
	May 30	Marra, et al., publish SARS-CoV sequence.
	Jun. 1	Last deaths from “natural” outbreaks.
	Oct. 3	Baric group publishes reverse genetics system with Urbani strain.
2004	Apr. 1	Yang, et al., publish DNA vaccine for SARS in a mouse model.

Sources: WebMD, WHO, *Science*, *Nature*, *J. Virology*



Examples of Small Organization Inventions

Source: US Small Business Administration

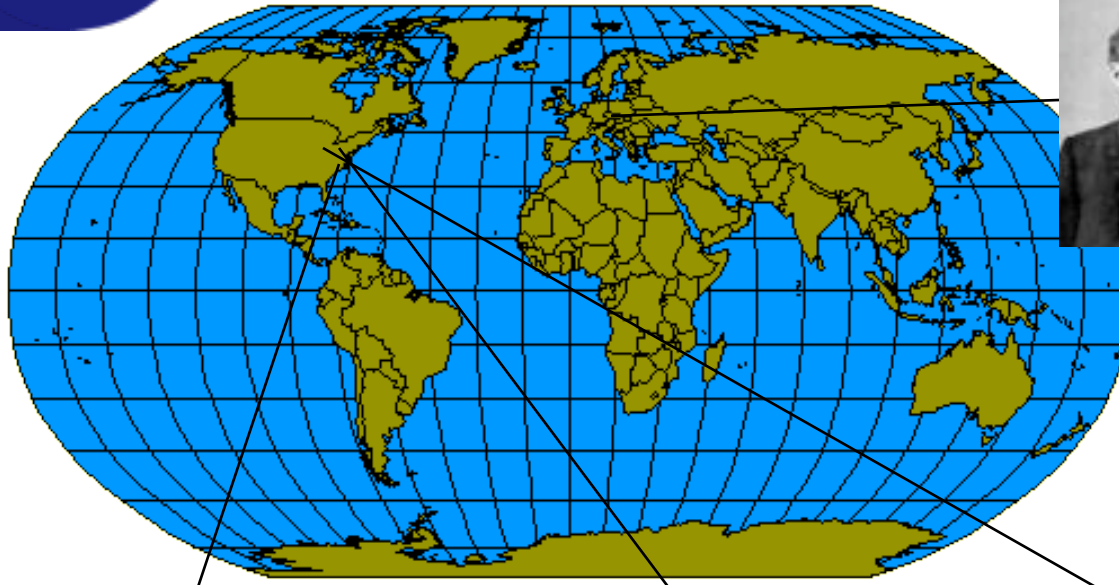
Air Conditioning
Air Passenger Service
Airplane
Articulated Tractor
Chassis
Assembly Line
Audio Tape Recorder
Bakelite
Biomagnetic Imaging
Biosynthetic Insulin
Catalytic Petroleum
Cracking
Cellophane
Artificial Skin
Computerized Blood
Pressure Controller
Continuous Casting
Cotton Picker
Defibrillator
DNA Fingerprinting
Double-Knit Fabric
Electronic Spreadsheet
Freewing Aircraft
FM Radio
Front-End Loader
Geodesic Dome

Gyrocompass
Heart Valve
Heat Sensor
Helicopter
High Resolution CAT
Scanner
High Resolution Digital
X-Ray
Human Growth Hormone
Hydraulic Brake
Integrated Circuit
Kidney Stone Laser
Large Computer
Link Trainer
Microprocessor
Microscope
NMR Scanner
Optical Scanner
Oral Contraceptives
Outboard Engine
Overnight National
Delivery
Pacemaker
Personal Computer
Photo Typesetting
Polaroid Camera

Portable Computer
Prestressed Concrete
Prefabricated Housing
Pressure Sensitive Tape
Programmable Computer
Quick-Frozen Food
Reading Machine
Rotary Oil Drilling Bit
Safety Razor
Six-Axis Robot Arm
Soft Contact Lens
Solid Fuel Rocket Engine
Stereoscopic Map
Scanner
Strain Gauge
Strobe Lights
Supercomputer
Two-Armed Mobile Robot
Vacuum Tube
Variable Output
Transformer
Vascular Lesion Laser
Xerography
X-Ray
X-Ray Telescope
Zipper



Technology Development is Distributed: Early Aviation



- Otto Lilienthal
- 1st flight in 1891
- Berlin



- Wright Brothers
- 1st flight in 1900



- Samuel Langley, 1903
- "Langley's Law"



- Octave Chanute
- 1890's
- Open Source Aviation



Synthetic Biology: Globally Distributed Capacity, c.2007

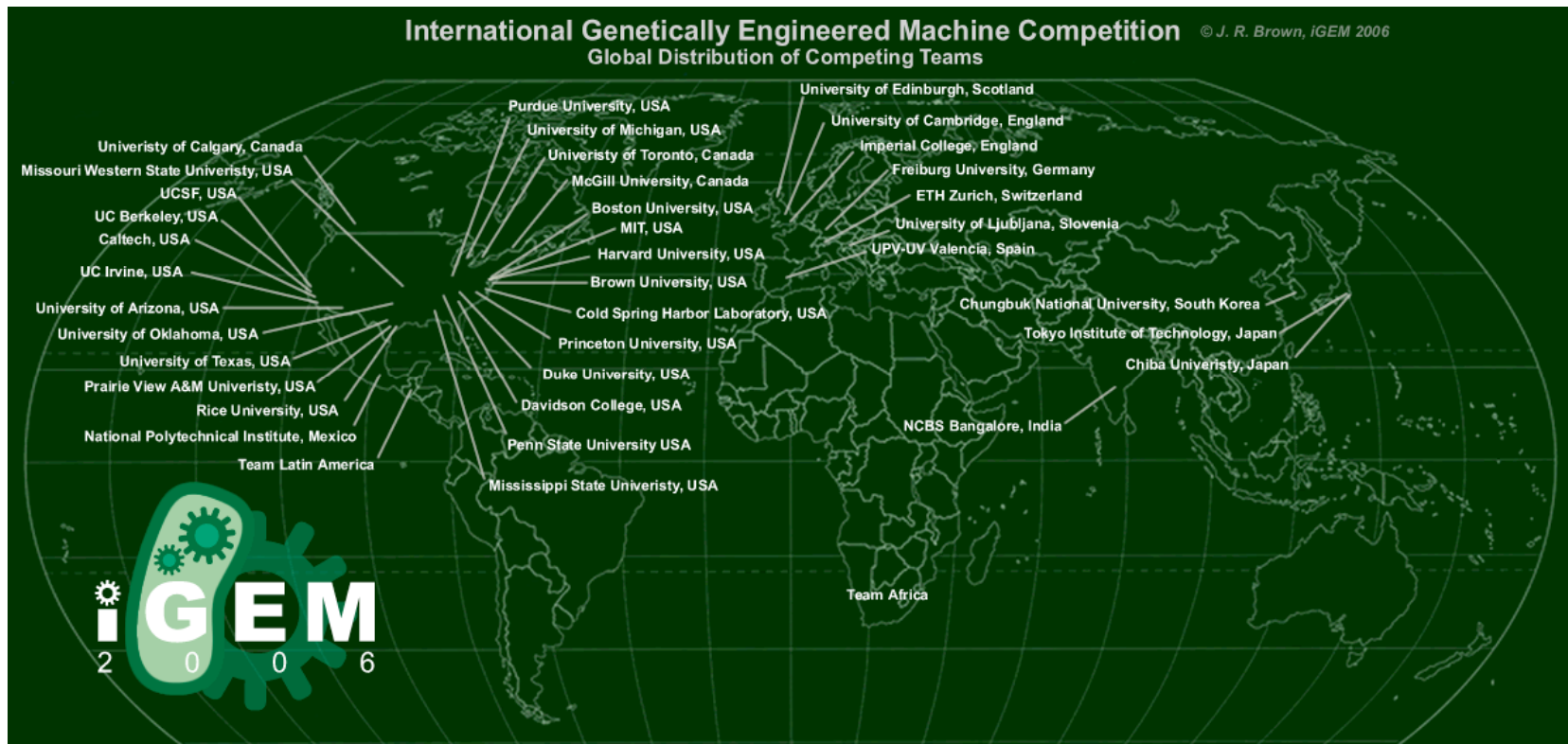
Gene Synthesis Foundries



Consolidation since 2007, but no technical or economic barriers to participation.



Synthetic Biology: Geographic Distribution of iGEM 2006 Competitors



iGEM 2005: Produced numerous papers.

iGEM 2006: First- and second-year university students built a system with ~20 components.

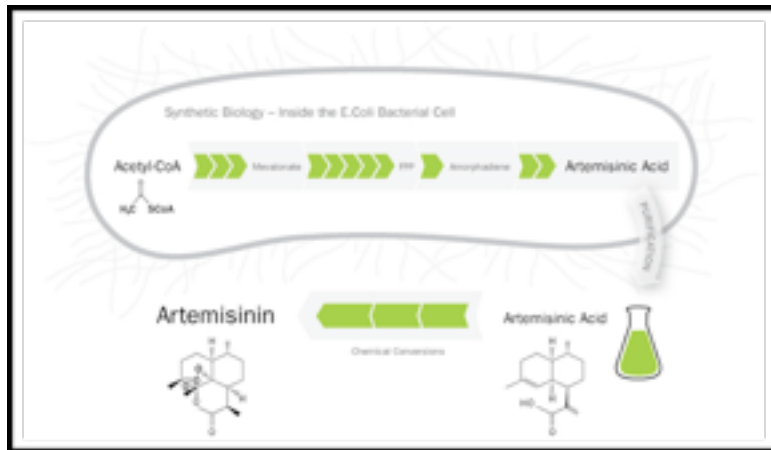
iGEM 2007: ~400 students from ~60 schools. Bio-energy makes first appearance; all parts in public domain.

iGEM 2008: ~1200 students (825@MIT), 77 presentations. Synthetic vaccines, hacked pro-biotics.

iGEM 2009: ~1200 students @MIT, 110 presentations. More fuels, manufacturing, bio-pixels.



How Many Genes Are Enough?



Artemisinin Project:

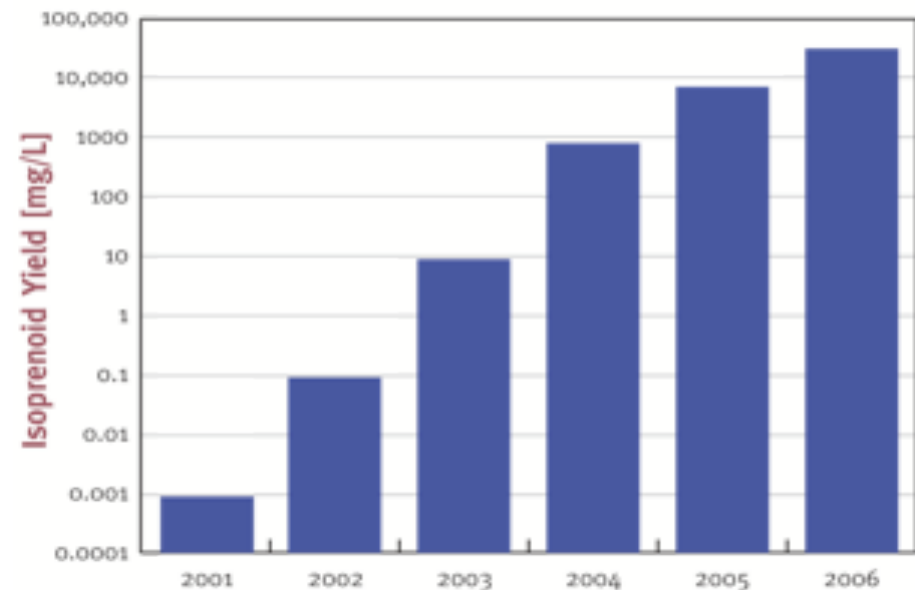
12 genes from 4 organisms

Now at tens of man-years of invested labor, >\$40 million

Not a portable hack

But led to Amyris and commercialized 2nd generation biofuels, ~Jan 2011.

Pre-Synthetic Biology Improvements in Isoprenoid Yield



Source: J. Keasling



Unexpected Impacts of Proscription

Methamphetamines:

“..Marked success in decreasing domestic methamphetamine production through law enforcement pressure and strong precursor chemical sales restrictions has enabled Mexican DTOs to rapidly expand their control over methamphetamine distribution.”

<http://www.usdoj.gov>

Increased enforcement efforts have created a larger, blacker market that is “[M]ore difficult for local law enforcement agencies to identify, investigate, and dismantle because [it is] typically much more organized and experienced than local independent producers and distributors.”

“Methamphetamine Strategic Findings”: <http://www.usdoj.gov>

Cocaine:



<http://blog.wired.com/27bstroke6/2009/01/new-law-harpoon.html>

Restricting access to commodities can create dedicated technology development efforts to meet supply:

- ➔ “Narco-subs”
- Cost of Construction: \$.5-2 million.
- Cargo: ~\$200 million in cocaine.
- Moved on to fully submersible?